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EXAMINER

STRZELECKA, TERESA E

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| ART UNIT | PAPER NUMBER |
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1637

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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| <p align="center">Office Action Summary</p> | <p>Application No.</p> <p>10/821,689</p> | <p>Applicant(s)</p> <p>WILLIAMS, JOHN G.K.</p> | |
| | <p>Examiner</p> <p>Teresa E. Strzelecka</p> | <p>Art Unit</p> <p>1637</p> | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 April 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-46 is/are pending in the application.
- 4a) Of the above claim(s) 4-17, 20, 21, 24, 25 and 27-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 18, 19, 22, 23 and 26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>4/30/07; 6/7/07</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This office action is in response to an amendment filed April 30, 2007. Claims 1-46 were previously pending, with claims 4-17, 20, 21, 24, 25 and 27-46 withdrawn from consideration. Applicant did not amend any claims. Claims 1-3, 18, 19, 22, 23 and 26 will be examined.
2. Applicant's arguments overcame the rejection of claims 1-3, 18, 19, 22, 23 and 26 under 35 U.S.C. 112, first paragraph, enablement. All other previously presented rejections are maintained for reasons given in the "response to Arguments" below.
3. This office action contains new grounds for rejection based on the IDS filed 4/30/07.

Information Disclosure Statement

4. The information disclosure statements (IDSs) submitted on April 30, 2007 and June 7, 2007 were filed after the mailing date of the non-final office action on December 28, 2006. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Response to Arguments

5. Applicant's arguments filed April 30, 2007 have been fully considered but they are not persuasive.

A) Regarding the interpretation of claim terms of "attachment complex", "anchor" "irreversible association" and "processivity index" Applicant argues that these terms are defined by examiner in a manner inconsistent with their ordinary and customary meaning given to the terms by one of ordinary skill in the art.

First, the examiner did not define the terms, but interpreted them. The term "processivity index" was specifically defined by Applicants, and it was used as such (see the Claim Interpretation section of the previous office action). Further, in view of the lack of the definitions for the other

Art Unit: 1637

terms, the interpretation provided by examiner is the broadest possible and reasonable interpretation which would be understood by one of ordinary skill in the art.

B) Regarding the rejection of claims 1-3, 18, 19 and 26 under 35 U.S.C. 102(b) as anticipated by Yao et al., Applicant argues that Yao et al. did not teach irreversible association of the polymerase with a target nucleic acid, since they teach that the PCNA clamp dissociates from the DNA in about 24 minutes.

However, Applicant did not define the term “irreversible association”, i.e. the time frame of the irreversibility. Therefore, in case of Yao et al., the association is irreversible for the 24 minutes of the reaction. Further, the claim is drawn to any nucleic acid molecule, either linear or circular. In case of a linear molecule, if it is shorter than the number of nucleotides which can be processed during a given reaction time, it will be irreversibly associated with the polymerase only during this time, since as the polymerase moves along the DNA, it will eventually reach its end.

The rejection is maintained.

Claim Interpretation

6. The term “attachment complex” has not been defined by Applicant, therefore it is considered as any molecule. Further, the term “polymerase has an attachment complex” is interpreted as “polymerase comprises an attachment complex” and the attachment complex may be covalently or non-covalently linked to the polymerase.

7. Applicant did not define the term “anchor”, therefore it is considered as any molecule.

8. Applicant did not define the term “irreversible association”, therefore, any association is considered as irreversible, provided the time scale or topological constraints.

9. Applicant defined the term “processivity index” on page 7, [0038], as the number of nucleotides sequenced divided by the number of nucleotides in the template.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-3, 18, 19 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Yao et al. (Genes to Cells, vol. 1, pp. 101-113, 1996).

Regarding claim 1, Yao et al. teach a polymerase-nucleic acid complex, where the polymerase comprises a gp45 clamp or a PCNA clamp (=attachment complex), which irreversibly associates the polymerase with the nucleic acid to increase processivity (page 111, last paragraph; page 112, paragraphs 1, 2 and 4; Abstract; page 104, third-fifth paragraphs; page 105, first paragraph; Fig. 3).

Regarding claim 2, Yao et al. teach a complex with a primer (page 111, last paragraph; page 112, first paragraph; page 104, third paragraph).

Regarding claim 3, Yao et al. teach that gp45 and PCNA have three subunits (= anchors) (page 101, first paragraph; page 102, first paragraph).

Regarding claim 18, Yao et al. teach circular DNA (page 111, last paragraph; page 112, first paragraph; page 104, third paragraph).

Regarding claim 19, Yao et al. teach that the circular DNA molecules were nicked (page 111, fifth paragraph), therefore they were inherently amplified by strand displacement.

Regarding claim 26, Yao et al. teach increased processivity of the polymerases with their processivity clamps (Abstract), and since the processivity depends of on the reaction conditions and

Art Unit: 1637

a specific template, it is inherent that the processivity of the polymerase with the clamp would be at least 0.5 with respect to the polymerase without the clamp.

12. Claims 1-3, 18 and 26 are rejected under 35 U.S.C. 102(a) as being anticipated by Motz et al. (J. Biol. Chem., vol. 277, pp. 16179-16188, May 2002; cited in the IDS).

Regarding claims 1 and 26, Motz et al. teach a Taq polymerase-nucleic acid complex, where the polymerase comprises a PCNA-binding domain and PCNA assembled on the binding domain (=attachment complex), which irreversibly associates the polymerase with the nucleic acid to increase processivity (Abstract; page 16180, second paragraph; page 16181, third and last paragraphs; page 16183, second paragraph; page 16186, second and third paragraphs; Fig. 4).

Regarding claim 2, Motz et al. teach primers for the target nucleic acid (page 16181; third paragraph).

Regarding claim 3, Motz et al. teach PCNA and the PCNA-binding domain, therefore they teach two anchors (page 16183, second paragraph).

Regarding claim 18, Motz et al. teach circular DNA (page 16181; third paragraph).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. Claims 19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Motz et al. (J. Biol. Chem., vol. 277, pp. 16179-16188, May 2002; cited in the IDS) and Blanco et al. (U.S.

Patent No. 5,198,543 A).

Art Unit: 1637

A) Motz et al. teach Taq DNA polymerase, but do not teach strand displacement synthesis or polymerases of claim 22.

B) Blanco et al. teach using phi29 DNA polymerase for strand displacement amplification and sequencing (col. 1, lines 9, 10; col. 2, lines 3-35; col. 4, lines 18-52; col. 8, lines 46-51 and 54-57).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the phi29 DNA polymerase of Blanco et al. as a polymerase of Motz et al. Blanco et al. specifically teach that phi29 polymerase can be used in place of a Taq polymerase (col. 8, lines 54-57). The motivation to do so, provided by Blanco et al., would have been that the polymerase did not require temperature cycling and produced long strands of DNA (col. 8, lines 46-51).

15. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Williams (U.S. Patent No. 6,255,083 B1) and Motz et al. (J. Biol. Chem., vol. 277, pp. 16179-16188, May 2002; cited in the IDS).

A) Regarding claim 23, Williams teaches sequencing of nucleic acids using DNA polymerases immobilized on solid supports and Klenow DNA polymerase (col. 2, lines 16-36; col. 14, lines 21-58) as well as Taq polymerase (col. 17, lines 43-58). Williams does not teach irreversible association of the polymerase with nucleic acid target.

B) Motz et al. teach a Taq polymerase-nucleic acid complex, where the polymerase comprises a PCNA-binding domain and PCNA assembled on the binding domain (=attachment complex), which irreversibly associates the polymerase with the nucleic acid to increase processivity (Abstract; page 16180, second paragraph; page 16181, third and last paragraphs; page 16183, second paragraph; page 16186, second and third paragraphs; Fig. 4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the modified Taq polymerase of Motz et al. in the nucleic acid sequencing method of Williams. The motivation to do so, provided by Motz et al., would have been that the modification increased the Taq polymerase processivity (page 16186, second paragraph; Fig. 4).

16. No claims are allowed.

Conclusion

17. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on April 30, 2007 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1637

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Teresa E Strzelecka
Primary Examiner
Art Unit 1637

Teresa Strzelecka
7/3/07